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(54) Title: INDUSTRIAL PROCESS FOR THE SYNTHESIS OF ISOBUTYL METHYL 1,4-DIHYDRO-2,6-DIMETHYL-4-(2-NITROPHENYL)-3,5-PYRIDINE DICARBOXYLATE (NISOLDIPINE)

(57) Abstract: Synthetic process of isobutyl methyl 1,4-dihydro-2,6-dimethyl-4-(2-nitrophenyl)3,5-pyridine dicarboxylate (Nisoldipine) comprising on the reaction of isobutyl 2-(2-nitrobenzylidene)acetoacetate with methyl 3-aminocrotonate in an apolar solvent.



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INTERNATIONAL SEARCH REPORT

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According to International Patent Classification (IPC) or to both national classification and IPC

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Minimum documentation searched (classification system followed by classification symbols)
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Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

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C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	US 4 154 839 A (BOSSERT FRIEDRICH ET AL) 15 May 1979 (1979-05-15) cited in the application example 1	1

☐ Further documents are listed in the continuation of box C:

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Patent document cited in search report	Publication date	Patent family member(s)	Publication date
US 4154839	A	15-05-1979	
		DE 2549568 A1	18-05-1977
		AT 352129 B	10-09-1979
		AT 814276 A	15-02-1979
		AU 498964 B2	29-03-1979
		AU 1935876 A	11-05-1978
		BE 847968 A1	04-05-1977
		BG 24668 A3	12-04-1978
		BG 25078 A3	12-07-1978
		BG 25079 A3	12-07-1978
		BG 24803 A3	12-05-1978
		BG 24804 A3	12-05-1978
		BG 24805 A3	12-05-1978
		CA 1085406 A1	09-09-1980
		CH 622779 A5	30-04-1981
		CH 623038 A5	15-05-1981
		CS 200500 B2	15-09-1980
		CS 200499 B2	15-09-1980
		DK 498476 A , B,	06-05-1977
		ES 452986 A1	16-12-1977
		ES 463166 A1	16-07-1978
		FI 763160 A , B,	06-05-1977
		FR 2330395 A1	03-06-1977
		GB 1516793 A	05-07-1978
		GR 61241 A1	12-10-1978
		HK 12681 A	10-04-1981
		IE 43984 B1	15-07-1981
		IL 50817 A	25-07-1979
		JP 1103097 C	25-06-1982
		JP 52059161 A	16-05-1977
		JP 56047185 B	07-11-1981
		LU 76133 A1	02-06-1977
		LU 88275 A9	03-02-1994
		NL 7612198 A , C	09-05-1977
		NO 763608 A , B,	06-05-1977
		NZ 182502 A	28-07-1978
		PL 106084 B1	30-11-1979
		PL 105940 B1	30-11-1979
		PT 65797 A , B	01-12-1976
		RO 70295 A1	17-08-1981
		SE 423542 B	10-05-1982
		SE 7612308 A	06-05-1977
		ZA 7606622 A	26-10-1977